THE USE OF IODIN IN THE TREATMENT OF DISEASES OF THE THYROID GLAND

HENRY ELSNER MARKS

(Summarized from the paper delivered before the New York Academy of Medicine May 21, 1925)

The empirical use of iodin in the treatment of goiter is of remote origin. In 1895 Baumann announced the discovery of iodin as a normal constituent of the thyroid gland and since that time innumerable attempts have been made to relate the various forms of thyroid disease to disturbances in iodin metabolism and to apply iodin, or iodin-containing desiccated normal glands, to the treatment of these disorders. Frequently, in hyperthyroidism, an exacerbation of symptoms followed such attempts and as a result clinical literature abounds with warnings against the use of iodin in exophthalmic goiter. Kocher taught that iodin must never be given and Mellanby states that in the discussion on the treatment of exophthalmic goiter at the Royal Society of Medicine in 1923 no speaker mentioned the use of iodin or any iodin preparation.

In 1909 Marine published his studies on the anatomy and physiology of the thyroid, showing the relation between iodin content, hyperplasia and colloid formation. He found that when the iodin content of the gland drops below .1% hyperplasia begins, and that when iodin is supplied regressive changes occur, the hyperplastic tissue reverting to colloid-filled vesicular tissue of the normal form. From this he concluded that a colloid goiter is a gland which was once hyperplastic but which has reverted to the resting stage without complete reversion to normal in size. In calling attention to the effect of iodin upon hyperplasia, he warned against the use of large doses, and showed that minute amounts of iodin are sufficient to bring about regression. The isolation by Kendall of the physiologically active iodin-bearing secretion of the thyroid gland in 1916 furnished the basis for further important studies of the quantitative relationship of iodin to thyroid activity. Such studies were made possible by

the use of the basal metabolic rate as a quantitative measure of thyroid activity, as initiated by DuBois. As a result of these studies Plummer has lately again called attention to the use of iodin in thyroid disease. He restricts its use to the pre-operative treatment of exophthalmic goiter and the treatment of post-operative reactions. He distinguishes between exophthalmic goiter with diffuse hyperplasia, in which he believes the thyroid product to be an abnormal thyroxin, and the circumscribed enlargements or adenomatous goiters which, when toxic, he believes elaborate an excessive amount of normal thyroxin. He also states that simple adenoma may become hyperactive when treated with iodin. His reason for using iodin only as preliminary to operation in exophthalmic goiter is that the control of symptoms by iodin cannot usually be maintained for more than a few weeks.

In studying the effect of iodin on patients with thyroid disease at the Vanderbilt Clinic, we determined to treat a series of cases with this agent for as long a period of time as it was possible to keep symptoms under control, and resort to surgery only if iodin and X-ray failed. Some of these patients were treated with iodin alone, others with both iodin and X-ray. In no case was it possible to secure complete relief from physical and mental stress. A few of the patients stopped working during the period when their symptoms were most pronounced, but aside from this they went about their usual activities.

Case 1. A woman admitted in August, 1922, age 64, with diabetes. Complained of weakness and nervousness. The thyroid showed circumscribed enlargement. No eye signs, no tremor. The heart was enlarged, B.P. 169/88, P.R. 132. Only the diabetes was treated at first. In February, March, April, May and September, 1924, and March, 1925, X-ray treatments were given. Lugol's solution was also given during parts of this time. Despite these measures the pulse rate has continued to range between 112 and 160 and the BMR from plus 20% to plus 48%. Subjective condition however is very much improved. Pulse rate still 140 but she looks healthy and well, and says she feels "all right." Operation recommended, but refused.

This is the only case in which we have as yet felt it necessary to recommend surgery, and here only because of the persistent

tachycardia. There are no other signs of thyroid intoxication, there is scarcely any enlargement of the gland, and there is considerable doubt as to whether the tachycardia is due to present hyperthyroidism.

Case 2. Man aged 33, with fairly typical exophthalmic goiter of three years duration. Nervousness, tremor and exophthalmos, with excessive perspiration. Pathological eye signs all present. P.R. 100. BMR plus 35%, with basal pulse rate during the test 108. The thyroid is soft and vascular, with moderate diffuse enlargement. There is little discrepancy between the usual pulse rate and the basal rate. After one week on Lugol's solution, ten drops daily, the P.R. dropped from 98 to 80, he felt stronger, less nervous, and had less palpitation, and the thyroid decreased a little in size. The iodin was now increased to 25 drops daily, and the patient's weight increased ten pounds in a month. With this increase in weight the pulse rate rose again and a ten days interruption of the iodin sent it up still further to 110. A series of four X-ray treatments over a period of ten weeks was now given, combined with resumption of iodin, with the result that the pulse rate dropped to 60, the thyroid became much smaller, the BMR fell to minus 15%, the weight rose again almost fifteen pounds, and the patient resumed work with practically no symptoms. For the past five months there has been no treatment. The weight has dropped again, but the P.R. is now 72, the BMR plus 10%, and the thyroid is just palpable. Exophthalmos is slight. If there are any future recurrences it will be interesting to see whether they can be as easily controlled.

Case 3. Man aged 35 whose illness began eleven weeks before admission with lachrymation, protrusion of the eyeballs and enlargement of the neck. Two weeks before admission shortness of breath and a feeling of obstruction in the throat. He had lost about fourteen pounds in a year. There was a very large soft vascular goiter without nodules, marked exophthalmos, tremor and nervousness. The P.R., however, was only 58 and the BMR was 14% below normal. BPR (Basal Pulserate) was 54. The body was apparently withdrawing thyroxin from the gland and destroying it faster than it could be replaced. No treatment was given. Two weeks later the picture had changed. The BMR was now plus 39% and the BPR 92. The thyroid seems now to have been actively producing a substance which was stimulating the metabolic rate. Lugol's was now started in doses of fifteen drops daily, and in three weeks the goiter had diminished markedly in size, the PR was 62, the BMR minus 1%, and the BPR 54. His symptoms had improved greatly. Lugol's was now discontinued. In one week the PR had risen to 66, after a second week without iodin it had gone up to 114, and he complained of substernal and precordial distress. He was put back upon iodin and has not yet returned to the clinic. In this case of acute hyperthyroidism we again see but little discrepancy between the basal pulse rate and the usual pulse rate.

Case 4. A woman of 77 years who has complained of enlargement of the eyes for the past six months. There is no perceptible thyroid enlargement, no sweating and little or no tremor. There is nervousness and insomnia, PR 96, the heart is enormously enlarged, 6 cm. to the right and 14 cm. to the left, B.P. 240/114. The radials are sclerotic, there is retinal sclerosis and evidence of diffuse hyperplastic sclerosis of the smaller vessels as well as decrescent arteriosclerosis. BMR was plus 35%, BPR 88. Lugol's was given at once, thirty minims daily, and within a few weeks the PR was 80, the weight increased four pounds, the BMR dropped to plus 10%, and the patient felt vastly better. At the eleventh week an intercurrent acute respiratory infection sent the PR up to 100 and the BMR up to plus 20%. Iodin was increased for one week, and the BMR again dropped to plus 5% and the BPR to 70.

This case is of interest, not only because of the advanced age of the patient, but because of the obscurity of the clinical picture, the immediate and complete response to iodin, the recurrence of symptoms when an intercurrent acute infection increased the demands of the body upon the thyroid, and the immediate and complete response again to an increase in iodin supply. Here again the discrepancy between BPR and usual PR was slight.

The next case is that of a patient with circumscribed enlargement of the thyroid and marked symptoms of sympathetic instability. Chief among these symptoms is a marked discrepancy between the usual PR and the pulse rate under basal conditions, with at the same time marked instability of the metabolic rate so that determination of the true basal rate is difficult, if not impossible. We have noted this syndrome in a number of patients with circumscribed or so-called adenomatous enlargement of the thyroid, but because of limitations of space only three will be cited here. The pulse rate under basal conditions is normal or only slightly elevated, but there is marked tachycardia under ordinary conditions. Tremor, nervousness, palpitation, sweating and insomnia are frequent, and there are often menstrual disturbances. Eye signs and exophthalmos are absent, or present only in slight degree. That the thyroid is implicated in this syndrome is suggested by the shrinkage of the gland and improvement in symptoms upon administration of iodin, but the marked instability of the PR as contrasted with cases of typical exophthalmic goiter indicates the presence of an added factor.

Case 5. A woman aged 45 with circumscribed enlargement of the thyroid, non-vascular. She is nervous and weak, and there are tremor, tachycardia, palpitation, insomnia, and glycosuria. No exophthalmos or eye-signs. B.P. 150/90. PR 120, BPR 80, BMR minus 8%. During the first five months of observation there were three peaks on the weight curve and these corresponded with the appearance of glycosuria and elevation of the pulse rate. Lugol's was then given, 15 drops daily for three weeks, and the PR dropped at once to 94 despite another increase in body weight. Interruption of iodin for six weeks resulted in a rise in PR to 110. Iodin was then resumed for three months, with disappearance of palpitation, insomnia and nervousness and reduction of the thyroid enlargement. During the 7 months since iodin was discontinued a moderate tachycardia has persisted, the PR varying from 94 to 106, but the thyroid enlargement has disappeared and the patient continues to feel well in all respects. The BPR remains at 80. The metabolic rate is still unstable and successive graphs, taken at intervals of only a few minutes, show marked variations.

Case 6. A woman aged 46 with circumscribed thyroid enlargement dating from her first pregnancy 12 years ago. Severe nervousness and palpitation began 1 year ago. PR 106, BPR 90, BMR plus 25%. Lugol's solution in doses of 10 drops daily for 2 weeks brought the PR down to 88, with improvement in the symptoms. Upon discontinuing iodin for 1 month the PR rose to 120, while 2 weeks after resuming it in doses of but 5 drops daily the PR dropped again to 70 and all nervousness disappeared. Iodin was continued in small doses and 7 months later the BMR was plus 1%, BPR 80 and PR likewise 80. The patient felt very well and there was no nervousness. She then had an attack of grippe and was in bed for 2 weeks with fever, during which time she stopped taking iodin. When she reappeared her PR was 115, BMR plus 29%, though the BPR remained at 80. Large doses of iodin in a week brought the BMR down to plus 6%, with PR and BPR both at 80. She feels and looks well and the thyroid is scarcely palpable.

This case again illustrates the effect of iodin upon this syndrome, with relief of symptoms, shrinkage of the thyroid enlargement, and stabilization of the pulse rate. It also shows again the effect of an intercurrent acute infection in increasing the demands of the body upon the thyroid.

Case 7. This woman first came to the clinic 12 years ago, at the age of 37, with severe diabetes. She had a moderate irregular enlargement of the thyroid, with nervousness, palpitation, tachycardia and tremor, the PR ranging between 100 and 130. During this entire period the symptoms remained about the same, no progression or improvement being noted. Over 2 years ago Syr. Ferrous Iodid was given for 1 month, with a drop

in PR from 130 to 100 and immediate rise again when the iodin was discontinued. Ten months later the BMR was plus 50%. Two X-ray treatments were now given and were followed by a drop in the BMR to minus 2%, with PR 100 and BPR 76. Two months later there was an increase in PR and Lugol's solution was then given for one month, the PR dropping from 132 to 92. The patient felt much better and the thyroid was much smaller, so iodin was stopped, although the PR continued to be unstable. Eight months later the BMR had risen to plus 10% and the BPR was 92. Lugol's solution was now given for one month in doses of 30 drops daily, following which the BMR dropped to minus 8%, the BPR to 80 and PR to 92. No thyroid enlargement could be made out and the patient felt well.

These patients are still under treatment. They cannot be said to be cured, for two reasons. In the first place, the thyroid may still remain incapable of responding when increased demands are made upon it, without a recurrence of symptoms. In the second place, there may be an underlying fault, outside the thyroid gland, which creates an excessive demand upon the thyroid. We feel, however, that our experience has shown that iodin is, at least in some cases, able to relieve the symptoms when they occur and avert the necessity for surgical treatment. Some cases have not responded so well to iodin, and until a much larger amount of material is available the continued treatment of these cases with iodin must be regarded as experimental. We wish, however, to emphasize that we have encountered no contraindications as yet to the continued use of iodin except failure to respond satisfactorily to it. We have not yet seen an increase in toxic symptoms follow upon the use of iodin, nor have we seen, in patients who responded to iodin at the outset, a later failure to respond.

ON THE MECHANISM OF INSULIN ACTION

ERNST FRIEDRICH MUELLER (Germany)
HERBERT J. WIENER

(Delivered before the New York Academy of Medicine May 21, 1925)

The vast amount of research work bearing upon carbohydrate metabolism and Diabetes Mellitus in particular which followed the epoch-making discovery of von Mehring and Minkowski in